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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 251508

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Application Number	Filed
10/576,813	December 4, 2006

First Named Inventor: Thomas Stiefel

Art Unit	Examiner
1794	Elizabeth A. Gwartney

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 51,860.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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July 18, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 2 forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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REASONS FOR PRE-APPEAL BRIEF REQUEST FOR REVIEW

Status of Claims

Claims 1-8, 16, 17, and 19-23 are pending and are the subject of appeal.

Summary of Claimed Subject Matter

The appealed claims are directed to a nutrition trace element composition, wherein one daily dose of the composition contains 1 mg-2 mg of selenium and 30 mg-100 mg of zinc as trace elements, and wherein iron is not contained as a trace element (see the specification at, e.g., page 12, lines 13-14 and lines 26-28). The appealed claims also are directed to a method of nutrition of humans, which comprises administering to a human a nutrition trace element composition comprising selenium and zinc, wherein the daily dose of the composition comprises 1 mg-2 mg of selenium and 30 mg-100 mg of zinc, and wherein the trace element iron is not administered to the human (see the specification at, e.g., page 12, lines 13-14 and lines 26-28, and the Examples).

Grounds of Rejection to be Reviewed

Claims 1-8, 16, and 19-23 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frankel ("Supplementation of Trace Elements in Parenteral Nutrition: Rationale and Recommendations"), in view of Giordano et al. (U.S. Patent 6,660,293).

Claim 17 is rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Frankel and Giordano et al., in further view of Ballevre et al. (U.S. Patent Application Publication No. 2003/0161863).

Reasons for Withdrawal of Rejection

The Office has failed to properly establish a *prima facie* case of obviousness. Moreover, even if the Office has properly established a *prima facie* case of obviousness, the Office has not accorded appropriate weight to the Rule 132 declarations of record, which rebut the *prima facie* case of obviousness.

1. The Combination of Cited References Does Not Disclose or Suggest the Claimed Invention

Frankel discloses supplementation of chromium, copper, manganese, selenium, and zinc for patients on total parenteral nutrition therapy (TPN). Frankel recommends a "minimum provision" of 50 mcg/day (i.e., 0.05 mg/day) of selenium (Frankel at page 587, fourth paragraph). Frankel recommends a minimum of 5 mg/day of zinc and discloses that as much as 10 mg/day of zinc can be provided. Frankel does not disclose a composition comprising 30 mg-100 mg of zinc.

Giordano et al. discloses a composition and method for prophylactic nutritional supplementation and therapeutic nutritional supplementation. The composition comprises carotenoids, vitamin E, vitamin D, vitamin C, thiamine, riboflavin, niacin, folic acid, pyridoxine, biotin, pantothenic acid, cobalamin, magnesium, manganese, zinc, selenium, chromium, copper, alpha lipoic acid, and lutein, but is free of added iron. The dose of selenium in the composition is about 80 μg to 120 μg (i.e., 0.08 mg to 0.120 mg), with a dose of 100 μg (i.e., 0.1 mg) being preferred (see, e.g., column 6, lines 1-5). The dose of zinc in the composition is about 20 mg to about 30 mg, with a dose of 25 mg being preferred (see, e.g., column 10, lines 14-19).

Ballevre et al. discloses an enteral nutrition composition comprising micronutrients, including selenium and zinc, but excluding iron. Specifically, the composition can comprise about 40 μg to about 100 μg (i.e., about 0.04 mg to about 0.1 mg) selenium and about 5 mg to about 10 mg zinc.

Independent claims 1 and 16, from which all the other pending claims depend, require a nutrition trace element composition which contains 1 mg-2 mg of selenium and 30 mg-100 mg of zinc in one daily dose of the composition. Frankel does not disclose the claimed selenium ranges with sufficient specificity to have led one of ordinary skill in the art to choose the claimed selenium amounts. In this respect, the minimum dose of 50 mcg/day of selenium disclosed in Frankel is *20 times less* than the minimum dose of selenium required by the appealed claims. There is no specific teaching or suggestion in Frankel to prepare a composition containing the relatively narrow range of relatively high selenium amounts as presently claimed.

Neither Ballevre et al. nor Giordano discloses or suggests a composition comprising 1-2 mg of selenium or provides any credible reason for one of ordinary skill in the art to have modified the selenium amount to be administered to a subject in accordance with Frankel, so as to result in the relatively narrow range of relatively high selenium amounts as presently claimed. The courts have held that there must exist some credible reason for one of ordinary skill in the art to combine the prior art teachings in the manner necessary to arrive at the claimed invention. See, e.g., *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418, 82 U.S.P.Q.2d 1385, 1396 (2007) (there is a need "to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"); *In re Kotzab*, 217 F.3d 1365, 1371, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000) ("Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."); *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998) ("In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.").

The only way in which the combined disclosures of the cited references can be considered as teaching or suggesting the present invention as defined by the appealed claims is through the use of hindsight, i.e., with the knowledge of the present application and the invention as claimed therein. It is impermissible for the Patent Office to engage in hindsight reconstruction of the claimed invention by using Appellant's invention as a template and selecting and combining elements from references to fill in that template. See *In re Gorman*, 933 F.2d 982, 18 U.S.P.Q.2d 1885 (Fed. Cir. 1991). As stated by the Federal Circuit: "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'" *Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988), quoting *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012, 217 U.S.P.Q. 193, 199 (Fed. Cir. 1983).

As a result, the Office has not properly established a *prima facie* case of obviousness, such that the obviousness rejections should be withdrawn.

2. *The Office Has Not Accorded Appropriate Weight to the Rule 132 Declarations of Record*

The Rule 132 declarations of Dr. Thomas Stiefel submitted on December 28, 2009, and August 13, 2010, demonstrate, *inter alia*, that compositions comprising selenium and zinc in the claimed amounts, which are well beyond the amounts recommended in the prior art, can be used to successfully treat intensive care patients so that their selenium values and zinc values are maintained at normal levels without inducing toxic side effects. For example, a composition developed by the Appellant called Syntrace®, which comprises a daily dose of 1 mg of selenium and a daily dose of 30 mg of zinc, produces normal levels of selenium in the blood and serum of patients, without inducing toxic side effects. The selenium dose in the Syntrace® composition is more than twice the daily dose recommended by the World Health Organization (i.e., 400 μg) as of the filing of present application. The claimed selenium and zinc amounts are in a range which, prior to the filing of the present application, one of ordinary skill in the art would have reasonably assumed would have resulted in toxic side-effects.

Accordingly, the surprising finding by the Appellant is that the beneficial dose range for selenium and zinc in the treatment of intensive care patients is much higher than the dose ranges recommended in the prior art for intensive care patients (see, e.g., Ballevre et al.). It is also surprising that a selenium dose within the claimed range produces normal levels of selenium in the blood and serum of patients and does not induce toxic side-effects.

According to the Office, Appellant has not demonstrated the criticality of the claimed selenium dosage. In this respect, the Office contends that the Rule 132 declarations do not provide an adequate factual showing of unexpected results because the tested samples described therein are not commensurate in scope with rejected claims. The Office also contends that the comparison samples described in the Rule 132 declarations do not represent the closest prior art.

When considering whether evidence is commensurate in scope with the claimed invention, Appellant is not required to show unexpected results over the entire range of properties possessed by a chemical compound or composition (see, e.g., *In re Chupp*, 816 F.2d 643, 646, 2 U.S.P.Q. 2d 1437, 1439 (Fed. Cir. 1987)). The results described in the Rule

132 declaration submitted on December 28, 2009 are reasonably commensurate in scope with the rejected claims, and the results described in the Rule 132 declaration submitted on August 13, 2010 directly correspond to the claimed composition.

With respect to the comparison samples, the comparison drug described in the Rule 132 declarations (i.e., Tracutil®) comprises a daily dose of 20 μg selenium and 3.27 mg zinc. Contrary to the assertion of the Office (see Office Action dated March 16, 2011, page 10, first paragraph), the daily dose of selenium in the Tracutil® composition is equivalent to 0.020 mg, not 0.002 mg. Thus, the Tracutil® composition contains a daily dose of selenium that is the same order of magnitude as, and is only 2.5 times smaller than, the daily dose of selenium disclosed in Frankel. Accordingly, the doses of selenium and zinc in the Tracutil® composition are reasonably commensurate in scope with the closest prior art (i.e., Frankel, which discloses a composition comprising a daily dose of at least 0.05 mg selenium and as much as 10 mg of zinc).

The Office argues that one of ordinary skill in the art would not have considered the results described in the present application and the Rule 132 declarations to be surprising or unexpected, because Frankel discloses that selenium doses as high as 724 mcg/day (i.e., 0.724 mg/day) have been administered to patients with no signs of toxicity (Frankel at page 587, first paragraph). Appellant notes that the very next sentence of Frankel states that toxic effects of selenium have been observed in patients consuming greater than 850 mcg/day (i.e., 0.850 mg/day) of selenium. Therefore, one of ordinary skill in the art clearly would have expected that selenium doses greater than 0.850 mg, such as the claimed dose range of 1 mg-2 mg, induces toxic side effects.

For the foregoing reasons, the obviousness rejections are not well-founded. The Office has not properly considered the obviousness issue in accordance with established legal precedent – both with respect to considering whether the combination of cited references discloses or suggests the claimed invention and with respect to properly considering the evidence of unexpected properties set forth in the Rule 132 declarations of record. Accordingly, the obviousness rejections should be withdrawn.